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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/823,240	03/30/2001	Frank B. Gertler	M0656/7064(HCL)	6318

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EXAMINER
MCKELVEY, TERRY ALAN

ART UNIT	PAPER NUMBER
1636	

DATE MAILED: 04/22/2003

15

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/823,240	GERTLER ET AL.	
	Examiner	Art Unit	
	Terry A. McKelvey	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *31 January 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-17,25-28,37,45,52,56,59,65,71,75,76,82 and 83* is/are pending in the application.

4a) Of the above claim(s) *1-17,26-28,37,45,52,56,59,65,71,75,76,82 and 83* is/are withdrawn from consideration

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *25* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☒ The proposed drawing correction filed on *25 November 2002* is: a)☒ approved b)☐ disapproved by the Examiner

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *4, 10* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 C.F.R. §§ 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 C.F.R. § 1.821(d). The application refers to sequences without the use of the correct identifier.

For example, at Figure 2, in the sequence inserts shown in the figure, the application sets forth sequences without sequence identifiers.

Applicants should carefully review the specification to identify and properly label each sequence that is referred to within the specification, including drawings. Sequences in drawings can be identified with a SEQ ID NO: in the Brief Description of the Drawings for the figure or be present in the figure itself. If one or more sequences are referred to in the specification that are not present in the Sequence Listing, then a new Sequence Listing, a new CRF diskette containing the Sequence Listing and a new statement that the two are the same and includes no new matter must be submitted in order to fully comply with the Sequence Rules.

Applicants are required to comply with all of the requirements of 37 C.F.R. §§ 1.821 through 1.825. *Any* response to this Office Action which fails to meet *all* of these requirements will be considered non-responsive. The nature of the noncompliance with the requirements of 37 C.F.R. §§ 1.821 through 1.825 did not preclude the continued examination of the application on the merits, the results of which are communicated below.

Election/Restrictions

Applicant's election without traverse of Group III, claim 25 in Paper No. 14, filed 1/31/03 is acknowledged. The applicant indicated that the election was with traverse, arguing that the Examiner omitted the identification of therapeutic Ena/VASP inhibitors from the description of Group III, claim 25 and that examining the method for identifying both inhibitors and activators represents a single invention and will not place an undue burden upon the Examiner. This argument is not considered to be a traversal because the absence of indication of inhibitors as part of the method of claim 25 was a mere accidental omission of that part of the description of the claim. It was always intended to be a part of Group III because it was not placed into a separate group. Therefore, there is

agreement that all of claim 25 will be examined as Group III. Because there is no other traversal other than that concerning the accidental omission, the applicant is not traversing the actual, intended restriction.

Claims 1-17, 26-28, 37, 45, 52, 56, 59, 65, 71, 75-76, and 82-83 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in Paper No. 14.

Drawings

The proposed drawing correction and/or the proposed substitute sheets of drawings, filed on 11/25/02 have been approved. A proper drawing correction or corrected drawings are required in reply to the Office action to avoid abandonment of the application. The correction to the drawings will not be held in abeyance.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 25 is rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted steps are: after identifying the putative Ena/VASP activator or inhibitor as an (actual) Ena/VASP activator or inhibitor, there is a missing step to identify the Ena/VASP activator or inhibitor as a therapeutic Ena/VASP activator or inhibitor, because "therapeutic" is an indication that the activator or inhibitor can be used in treatment of a disease or condition, and identification of a biological activity of a compound does not mean that it can necessarily be used as a therapeutic. Alternatively, the claim may be unclear as follows.

Claim 25 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The preamble of claim 25 indicates that it is a method for identifying a therapeutic Ena/VASP activator or inhibitor. However, the method steps only result in the identification of Ena/VASP activators or inhibitors. Either there is a missing step for the reasons described above or it is unclear what is

intended by the claimed method: identification of therapeutic Ena/VASP activators and inhibitors as indicated by the preamble, or merely identification of (actual) Ena/VASP activators or inhibitors from putative Ena/VASP activators or inhibitors. It appears that the applicant intended the latter and the claim was examined as such.

Also, claim 25 recites "putative Ena/VASP activator or inhibitor" which renders the claim vague and indefinite because the metes and bounds of what is considered to be putative ENA/VASP activators or inhibitors is unclear. Does the phrase encompass any compound, in which case the claimed method reads on all prior art assays using mammalian cells to assay compounds that affect cell migration? Or, does the phrase only encompass those compounds that are reasonably hypothesized to be likely Ena/VASP activators or inhibitors based upon some other property of the compounds, such as binding to Ena/VASP (described at page 53 of the specification). Amending the claim to more clearly indicate the metes and bounds of putative Ena/VASP activators or inhibitors would be remedial.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claim 25 is rejected under 35 U.S.C. 103(a) as being unpatentable over Gertler et al (WO 98/01755, Applicant reference B1) in view of Clark et al (U.S. Patent No. 5,935,850).

Gertler et al teach that the Mena and Evl proteins (members of the Ena/VASP family) are involved in cell migration or motility. These proteins are disclosed as being useful for generating, isolating, and characterizing additional endogenous and exogenous factors, drugs, and other agents useful for evaluating and/or controlling cytoskeletal dynamics involved in normal and abnormal cell morphology, adhesion, motility, growth and/or differentiation. Reflective of these uses, the invention provides several methods and tools specifically directed to the diagnosis and treatment of injury and disease conditions involving cytoskeletal dynamic processes, such as metastatic cancer and infection by cytopathogenic bacteria (page 5). (The underlining was added by the Examiner for emphasis.) Among the Mena and Evl proteins disclosed are those that encode discrete functional domains of Mena and Evl which are responsible for specific biological activities of the intact protein, and analogs which exhibit modified biological activity (pages 5-6). Mena and Evl expression constructs are taught as being employed in methods for modulating expression of Mena or Evl, disrupting Mena or Evl expression or inducing ectopic expression of Mena or Evl genes and related polynucleotide sequences in mammalian host cells (page 6). Thus, these proteins are putative Ena/VASP activators or inhibitors. Gertler et al also teach that "In

other related screening and diagnostic methods, Mena or Evl based synthetic peptides, recombinantly produced peptides, fusion proteins and the like incorporating all or a portion of Mena or Evl, as well as mutant analogs of Mena or Evl proteins or peptides, are used to screen for specific agonists and antagonists of Mena or Evl activities (page 8). The reference also teaches that "The activity of N-Mena and other functional domains of Mena and/or Evl in cytoskeletal dynamic processes can be further evaluated and incorporated within the methods of the invention using a variety of additional tools that are disclosed herein, or are elsewhere described and known in the art." (page 15). Finally, Gertler et al teach "Screening for modulators of Mena or Evl expression or activity in the context of pathogenic infection is a particularly useful method, both in terms of the simplicity of the assay systems available, as well as in terms of the anticipated utility of the modulators that may be uncovered in such screens. In this context it is important to note that the Listeria monocytogenes organism is only one of many diverse pathogens that rely on the induction of host cytoskeletal dynamic processes for pathogenicity. The ability to grow in a host cell cytoplasm accompanied by actin-based movement and cell-to-cell spreading has also been observed for

the closely related pathogen Listeria ivanovaii and is shared by two other groups of pathogenic bacteria (page 26).

Gertler et al do not specifically teach determining the effect of the putative Ena/VASP activators or inhibitors taught by the reference on cell migration (as the assay) to identify actual Ena/VASP activators or inhibitors.

Clark et al teach an in vitro cell migration model using mammalian host cells and a method of using the cell migration model to screen substances for the effect of such substances on cell migration (throughout the reference, including columns 21-24).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to use the Mena or Evl mutant proteins or antibodies which are potential Ena/VASP activators or inhibitors taught by Gertler et al in the in vitro cell migration assay using mammalian cells taught by Clark et al because Gertler et al teach that it is within the ordinary skill in the art to use those proteins for evaluating cytoskeletal dynamics involved in cell motility and for screening for specific agonists and antagonists of Mena or Evl activities, that a variety of additional tools that are elsewhere described and known in the art can be used, and that screening for modulators of Mena or Evl activity in the context of pathogenic

infection (which involves cell movement) is a particularly useful method, and Clark et al teach that it is within the ordinary skill in the art to use an in vitro cell migration assay to screen for substances that affect cell migration.

One would have been motivated to do so for the expected benefit of creating an assay for identifying agonists and antagonists of Mena or Evl (i.e., Ena/VASP activators or inhibitors) using the mutant Mena or Evl proteins taught by Gertler et al which are putative Ena/VASP activators or inhibitors in a screening method for modulators of Mena or Evl activity in the context of pathogenic infection (which involves cell movement) which is taught by Gertler as a particularly useful method, using the convenient in vitro method taught by Clark et al. Based upon the teachings of the cited the references, the high skill of one of ordinary skill in the art, and absent evidence to the contrary, there would have been a reasonable expectation of success to result in the claimed invention.

Conclusion

No claims are allowed.

Certain papers related to this application may be submitted to Art Unit 1636 by facsimile transmission. The faxing of such

papers must conform with the notices published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 C.F.R. § 1.6(d)). The official fax telephone numbers for the Group are (703) 308-4242 and (703) 305-3014. NOTE: If Applicant *does* submit a paper by fax, the original signed copy should be retained by applicant or applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED so as to avoid the processing of duplicate papers in the Office.

Any inquiry concerning rejections or other major issues in this communication or earlier communications from the examiner should be directed to Terry A. McKelvey whose telephone number is (703) 305-7213. The examiner can normally be reached on Monday through Friday, except for Wednesdays, from about 7:30 AM to about 6:00 PM. A phone message left at this number will be responded to as soon as possible (i.e., shortly after the examiner returns to his office).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. Remy Yucel can be reached on (703) 305-1998.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Terry A. McKelvey, Ph.D.
Primary Examiner
Art Unit 1636

April 21, 2003